Remarks

Claims 2-13, 16, 18-22, 26, 40, 44, 62, 80, 98, 114, and 120 were pending. Claims 2-12, 16, 20, 22, 26, 40, 44, 62, 80, 98, 114, and 120 have been withdrawn from consideration. By this Amendment claims 13 and 21 are currently amended; new claims 121 and 122 are added; and no claims are canceled. No new matter is introduced.

New claims 121 and 122 depend from claims 19 and 21, respectively, and specify the host cell is a 293 fibroblast cell. Support for these claims can be found throughout the specification, including, for example, page 39, line 11, Example 2 beginning at page 97, and Example 10 beginning at page 106.

Applicant acknowledges that the Examiner has indicated that the previous objections to the specification and claim rejections under 35 U.S.C. § 112, second paragraph, and 35 U.S.C. § 102 have been withdrawn.

Information Disclosure Statement

Applicant wishes to call to the attention of the Examiner the existence of an Information Disclosure Statement (IDS) filed with the Patent Office on January 26, 2004. This IDS includes a Form 1449 with a reference not yet checked off by the Examiner. Applicant requests the Examiner to consider the reference cited therein and indicate such reference has been considered by the Examiner in any response to this paper.

Claim Rejections Under 35 U.S.C § 112, first paragraph

The Examiner maintained her rejection of claims 13, 18, 19, and 21 under 35 U.S.C § 112, first paragraph, for alleged lack of adequate written description. Specifically, the Examiner indicated that, although SEQ ID NOs 1, 2, 3, 4, and 141 meet the written description provision of 35 U.S.C § 112, first paragraph, claims 13, 18, 19, and 21 are directed to encompass a sequence that is not exactly listed in the specification and, further, that the polypeptide hTLR9-CXXCm is encoded by a nucleic acid not fully disclosed in the specification, claims, or drawings as originally filed. The Examiner went on to conclude that neither the polypeptide hTLR9-CXXCm

nor the nucleic acid encoding the polypeptide hTLR9-CXXCm meets the written description provisions of 35 U.S.C § 112, first paragraph.

Applicant respectfully disagrees and requests reconsideration and withdrawal of the rejection of claims 13, 18, 19, and 21 under 35 U.S.C § 112, first paragraph, in view of the current amendment of claim 13 and the following remarks.

Claim 13 as currently amended is drawn to an isolated nucleic acid molecule which encodes a Toll-like receptor 9 (TLR9) polypeptide hTLR9-CXXCm, said polypeptide comprising an amino acid sequence of SEQ ID NO:6 except for substitution of amino acids 269-274 (PRHFPQ) of SEQ ID NO:6 with amino acids 269-274 (GQKSLH) of SEQ ID NO:3. Support for this amendment can be found, for example, at page 106, lines 25-30, page 107, line 11, and Table 4, pages 94-96. SEQ ID NO:6 provides an amino acid sequence for full-length human TLR9. SEQ ID NO:3, already acknowledged by the Examiner to meet the written description requirement, provides an amino acid sequence for full-length murine TLR9. Claim 13 as currently amended thus specifies that polypeptide hTLR9-CXXCm has an amino acid sequence of human TLR9 (SEQ ID NO:6) save for substitution of amino acids 269-274 of human TLR9 with corresponding amino acids 269-274 of murine TLR9 (SEQ ID NO:3). Applicant submits that this is fully consistent with the disclosure in Example 10, appearing at pages 106-107 of the specification. Specifically, the specification in Example 10 discloses that by the use of a site-specific mutagenesis kit six amino acid residues (human: PRHFPQ 269-274; mouse: GQKSLH 269-274) were interchanged between human and murine TLR9 to create, inter alia, hTLR9-CXXCm. There is thus no question as to what is the amino acid sequence of the polypeptide hTLR9-CXXCm. In view of the foregoing, Applicant submits that the specification provides adequate written description of the amino acid sequence of the polypeptide hTLR9-CXXCm because amino acid sequences of human and murine TLR9 are fully disclosed and the particular amino acid residues that are interchanged between them are expressly set forth both in position and in sequence.

As noted above, Claim 13 as currently amended is directed to an isolated nucleic acid molecule which encodes a Toll-like receptor 9 (TLR9) polypeptide hTLR9-CXXCm. It is

Applicant's position that the claimed invention has adequate written description, for the following reasons:

First,

- The Examiner has already indicated that SEQ ID NOs 1 and 2, providing nucleotide sequences encoding full-length murine TLR9, satisfy the written description requirement;
- The Examiner has already indicated that SEQ ID NO:4, providing a nucleotide sequence encoding full-length human TLR9, satisfies the written description requirement;
- The Examiner has already indicated that SEQ ID NO:141, providing a nucleotide sequence described below, satisfies the written description requirement;
- As noted above, Applicant believes the polypeptide hTLR9-CXXCm has adequate written description;
- SEQ ID NO:141, found in Example 10 at page 106, line 31, provides a nucleic acid sequence used to modify nucleic acid encoding hTLR9 to include sequence encoding mouse GQKSLH at amino acid residues 269-274. This oligonucleotide includes human nucleic acid sequence flanking, on each side, the murine nucleic acid sequence encoding GQKSLH at amino acid residues 269-274. One of skill in the art would recognize that this sequence provided by SEQ ID NO:141 would correspond to and take the place of, for example, bases 936 - 980 provided in SEQ ID NO:4 or bases 1426-1470 provided in SEQ ID NO:5 (nucleic acid sequences of human TLR9); and
- Thus SEQ ID NO:4, modified to incorporate SEQ ID NO:141 at bases 936-980, as described in Example 10, provides adequate written description for a nucleic acid molecule which encodes a Toll-like receptor 9 (TLR9) polypeptide hTLR9-CXXCm, as claimed.

Second, in case the Examiner should take the view that the foregoing does not overcome the rejection, it is submitted that a specified amino acid sequence can serve as sufficient written description basis for a nucleotide sequence encoding the amino acid sequence. While it is true that degeneracy of the genetic code allows for multiple possible nucleic acid sequences encoding a specified amino acid sequence, it is nevertheless sufficient to know the amino acid sequence in

order to be able to specify each and every possible nucleic acid sequence encoding that amino acid sequence. In this instance, where it is the position of the Applicant that the amino acid sequence of hTLR9-CXXCm polypeptide is clear from the specification, Applicant is of the view that the described amino acid sequence of hTLR9-CXXCm serves as sufficient written description basis for the claimed nucleotide sequence encoding the hTLR9-CXXCm polypeptide.

Third, as to the Examiner's citation of Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, Applicant respectfully points out that Example 10 makes clear to those of skill in the art that, as of the filing date sought, Applicant was in possession of the invention, i.e., an isolated nucleic acid encoding hTLR9-CXXCm polypeptide, said polypeptide comprising an amino acid sequence of SEQ ID NO:6 except for substitution of amino acids 269-274 of SEQ ID NO:6 with amino acids 269-274 of SEQ ID NO:3. This is clear because, for example, the claimed nucleic acid sequence does not occur in nature and the Applicant expressed and characterized the hTLR9-CXXCm polypeptide as shown in Example 10 and Figure 20. Accordingly, the facts of the instant application distinguish over Vas-Cath Inc. v. Mahurkar.

Fourth, as to the Examiner's citation of Fiers v. Revel, 25 USPQ2d 1601, 1606, and Amgen Inc. v. Chugai Pharmaceutical Co. Inc., 18 USPQ2d 1016, Applicant respectfully points out that unlike in either of the recited cases, claim 13 as currently amended refers to a specific amino acid sequence encoded by the claimed nucleic acid molecule. By contrast, Revel sought to claim any DNA encoding a polypeptide identified only by its name (β-IF) and its function, at a time when the amino acid sequence of β-IF was not previously known. Similarly, by contrast, Amgen sought to claim genes encoding putative EPO analogs, at a time when the amino acid sequence of EPO was not previously known. Unlike Fiers v. Revel and Amgen Inc. v. Chugai Pharmaceutical Co. Inc., in the present application the Applicant clearly describes more than a mere wish or plan for obtaining a particular DNA because, as mentioned above, Applicant clearly had possession of the claimed DNA at the time of the claimed invention. Accordingly, the facts of the instant application distinguish over Fiers v. Revel and Amgen Inc. v. Chugai Pharmaceutical Co. Inc.

Applicant therefore respectfully requests the Examiner to reconsider and withdraw the rejection of claims 13, 18, 19, and 21 under 35 U.S.C § 112, first paragraph, for alleged lack of adequate written description.

Claim Rejections Under 35 U.S.C § 112, second paragraph

The Examiner rejected claim 21 under 35 U.S.C § 112, second paragraph, for alleged failure to particularly point out and distinctly claim the subject matter the Applicant regards as the invention. According to the Examiner, the phrase "Toll-like receptor (TLR)-related signaling" is vague and indefinite. More specifically, the Examiner alleges that is unclear what requirements and to what degree these requirements must be met in order to qualify as being "related" to TLR.

Without meaning to cede the Examiner's basis for the rejection, and without so doing in order to overcome prior art, Applicant has currently amended claim 21 to be directed to the host cell of claim 19, further comprising a reporter gene construct comprising a reporter gene operatively linked to a promoter sensitive to NF-κB. Support for this amended claim language can be found, e.g., at page 85, lines 6-12. As disclosed at page 85, lines 13-22, such reporter genes can include, for example, genes encoding an enzyme, a bioluminescence marker, a surface-expressed molecule, and secreted molecules. Also as disclosed at page 85, lines 13-22, such promoters sensitive to NF-κB include, for example, promoters for NF-κB, IL-1β, IL-6, IL-12 p40, CD80, CD86, and TNF-α.

Applicant believes that claim 21 as currently amended overcomes the rejection. Accordingly, Applicant respectfully requests the Examiner to reconsider and withdraw the rejection of claim 21 under 35 U.S.C § 112, second paragraph.

Summary

Claims 13 and 21 are amended and new claims 121 and 122 are added by this Amendment. It is believed that the claims are in condition for allowance. A prompt and favorable action is earnestly solicited.

If the Examiner has any questions about this response, she is urged to contact Applicant's representative at the number shown below.

Respectfully submitted,

Bauer et al., Applicant

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Attorney's Docket No. C1041.70016US00
Date: July 16, 2004
x08/05/04x